Ziopharm Oncology Announces Publication of Positive Results of Phase 1 Monotherapy Trial of Controlled IL-12 in Patients with Recurrent Glioblastoma in Science Translational Medicine

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– Ad-RTS-hIL-12 plus 20 mg veledimex (Controlled IL-12 platform) determined to be the preferred dose with low-dose steroids to treat adult patients with recurrent glioblastoma –
– Median overall survival for Controlled IL-12 in patients receiving low-dose steroids was 17.8 months –
– Increased tumor infiltrating lymphocytes and PD-1 (programmed cell death protein 1) support immunological anti-tumor effect of Controlled IL-12 –

BOSTON, Aug. 14, 2019 (GLOBE NEWSWIRE) -- Ziopharm Oncology, Inc. ("Ziopharm" or the "Company") (Nasdaq: ZIOP), today announced the publication of its phase 1 trial of Controlled IL-12 in patients with recurrent glioma in the journal *Science Translational Medicine*. The publication entitled, "Regulatable interleukin 12 gene therapy in patients with recurrent high-grade glioma: results of a phase 1 trial" can be accessed at https://stm.sciencemag.org/.

While IL-12 is known as a potent immune activator that triggers T cells to target cancer, historic trials systemically infusing IL-12 protein have failed due to intolerable toxicity. In contrast, this study showed that a ligand-inducible gene switch regulates expression of IL-12 from the central nervous system, resulting in increased cytokine and T-cell activity within the tumor environment, while preserving a favorable safety profile.

Glioblastoma is an aggressive, largely incurable cancer. Patients receive surgery, radiation and chemotherapy, but in almost all cases, tumors return within months. When this brain cancer recurs, median overall survival is six to nine months.[1,2]

The paper includes data from 31 patients with recurrent glioblastoma (rGBM) treated with Controlled IL-12 (Ad-RTS-hIL-12 plus veledimex, Ad+V). Frequency and severity of adverse events, including cytokine release syndrome, correlated with the veledimex (ligand) dose, reversing promptly upon discontinuation. The 20 mg veledimex dose had superior drug compliance and demonstrated 12.7 months median overall survival (mOS) at a mean follow-up of 13.1 months. Concurrent corticosteroids negatively impacted survival and patients had further improved mOS of 17.8 months when cumulative amount of dexamethasone was limited to less than 20mg during active veledimex dosing.

"I would like to thank the site teams and investigators, as well as all of the patients who participated in this trial," said Laurence Cooper, M.D., Ph.D., CEO of Ziopharm, "This study demonstrated that our Controlled IL-12 platform as monotherapy provides rapid activation of the immune system and is associated with improved overall survival for patients with rGBM, with a favorable safety profile. In addition, the upregulation of PD-1 expression seen upon repeat biopsies in this study supports the decision to pursue our ongoing trials combining Controlled IL-12 with inhibitors to programmed death-1 (PD-1)."

"In a phase 1 trial, we strive to show that a new drug candidate is first and foremost safe for patients and at the same time, aim to demonstrate initial evidence of efficacy," said corresponding author Antonio Chiocca, M.D., Ph.D., lead author and Chairman of Neurosurgery and Co-Director of the Institute for the Neurosciences at Brigham and Women's Hospital, Professor of Neurosurgery at Harvard Medical School, and Surgical Director of the Center for Neuro-oncology at Dana-Farber Cancer Institute. "We believe these study results show it is now possible to have regulatable immunotherapy via genes. Controlled IL-12 is well-tolerated in patients with glioblastoma, with encouraging evidence that the drug is having its intended effect."

"Glioblastoma at recurrence is a devastating cancer with few treatment options that have demonstrated success. These updated data show a promising extension of patients' survival and demonstrate how controlling the powerful cytokine IL-12 can engage the body's own immune system to generate an anti-tumor response against rGBM," said co-author Rimas V. Lukas, M.D., Associate Professor of Neurology (Neuro-Oncology), Northwestern University Feinberg School of Medicine and Department of Neurology, University of Chicago.

About Controlled IL-12 (Ad-RTS-hIL-12 plus veledimex)
Ziopharm's Controlled IL-12 platform is an investigational gene therapy designed to induce and control the production of human interleukin 12 (hIL-12) a master-regulator of the immune system. The Company has treated more than 100 patients, including more than 75 patients with rGBM, with Ad-RTS-hIL-12 plus veledimex and administered more than 1,300 doses of veledimex across three types of solid tumors, building a significant safety profile, mechanistic dataset and evidence of anti-tumor effects.

The Company announced earlier this year the completion of the enrollment in an "Expansion Substudy" (Clinicaltrials.gov NCT03679754) that enlarged the phase 1 trial by an additional 36 patients with Ad-RTS-hIL-12 plus 20mg/day veledimex for up to 14 days. In that cohort, 75% of patients (27/36) received low-dose steroids.

About Controlled IL-12 in combination with PD-1 inhibitors
Ziopharm is also advancing Ad-RTS-hIL-12 plus veledimex for the treatment of rGBM in combination with immune checkpoint inhibitors. In June 2019, the Company announced it had completed enrollment in three dosing cohorts in a phase 1 study of adult patients with rGBM to evaluate a single dose

of Ad-RTS-hIL-12 plus daily veledimex in combination with OPDIVO (nivolumab), an immune checkpoint inhibitor against PD-1 (Clinicaltrials.gov NCT03636477). Based on a favorable safety profile, investigators from this multi-center trial indicated interest in expanding the study and the Company now expects to enroll up to 12 additional patients at the highest dosing level.

The Company announced in June 2019 the initiation of a phase 2 trial evaluating the combination of Ad-RTS-hIL-12 plus veledimex with PD-1 antibody Libtayo® (cemiplimab - rwlc) for the treatment of recurrent or progressive glioblastoma (rGBM) in adults. The multi-center trial will be conducted at approximately 10 hospitals specializing in the treatment of brain cancers in the United States. The open-label, single-arm phase 2 trial will enroll approximately 30 patients with rGBM, with the primary endpoints being safety and efficacy.

Fast Track and Orphan Medicinal Product Designations
In April 2019, Ziopharm announced that the FDA had granted Fast Track designation for the Company's Controlled IL-12 program for the treatment of rGBM in adults. In August 2019, European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP) adopted a positive opinion recommending Controlled IL-12 for designation as an orphan medicinal product for the treatment of glioma.

Learn more about Controlled IL-12 online at https://ziopharm.com/controlled-il-12.

[1.] C. Kamiya-Matsuoka, M. R. Gilbert, Treating recurrent glioblastoma: an update. CNS Oncol 4, 91-104 (2015).
[2.] M. M. Mrugala, Advances and challenges in the treatment of glioblastoma: a clinician's perspective. Discov Med 15, 221-230 (2013).

About Ziopharm Oncology, Inc.
Ziopharm Oncology is an immuno-oncology company focused on developing end-to-end cost-effective solutions using its non-viral *Sleeping Beauty* platform for TCR and CAR T-cell therapies and immune-stimulating gene therapy with Controlled interleukin 12 (IL-12). The *Sleeping Beauty* platform genetically modifies T cells with DNA plasmids to express T-cell receptors (TCRs) to target neoantigens inside and outside hotspots for solid tumors and chimeric antigen receptors (CARs) to target CD19 for blood cancers using the Company's "rapid personalized manufacturing" to produce CAR-T within two day of gene transfer. The *Sleeping Beauty* platform is being advanced in collaboration with the National Cancer Institute, The University of Texas MD Anderson Cancer Center and Eden BioCell. The Company also is developing its Controlled IL-12 platform, or Ad-RTS-hIL-12 plus veledimex, as monotherapy and in combination with immune checkpoint inhibitors to treat brain cancer, including in collaboration with Regeneron Pharmaceuticals.

Forward-Looking Statements Disclaimer
This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts, and in some cases can be identified by terms such as "may," "will," "could," "expects," "plans," "anticipates," and "believes." These statements include, but are not limited to, statements regarding the Company's business and strategic plans and the progress and timing of the Company's research and development programs, including patient enrollment expectations. Although Ziopharm's management team believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Ziopharm, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, changes in our operating plans that may impact our cash expenditures, the uncertainties inherent in research and development, future clinical data and analysis, including whether any of Ziopharm's product candidates will advance further in the preclinical research or clinical trial process, including receiving clearance from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies to conduct clinical trials and whether and when, if at all, they will receive final approval from the U.S. FDA or equivalent foreign regulatory agencies and for which indication; the strength and enforceability of Ziopharm's intellectual property rights; competition from other pharmaceutical and biotechnology companies as well as risk factors discussed or identified in the public filings with the Securities and Exchange Commission made by Ziopharm, including those risks and uncertainties listed in Ziopharm's Quarterly Report on Form 10-Q filed by Ziopharm with the Securities and Exchange Commission. We are providing this information as of the date of this press release, and Ziopharm does not undertake any obligation to update or revise the information contained in this press release whether as a result of new information, future events or any other reason.

Ziopharm Contact:
Chris Taylor
VP, Investor Relations and Corporate Communications
617.502.1881
ctaylor@ziopharm.com

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